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Review Article

Early intervention and cumulative life course impairment in psoriasis: a review

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Abstract

Psoriasis is a chronic, systemic, inflammatory disease affecting the skin, joints and other organs. Psoriasis negatively affects patients' quality of life, causing social anxiety and negative coping, thus determining a cumulative life course impairment (CLCI). The concept of CLCI in psoriasis is reinforced by the understanding that psoriasis-associated comorbidities and stigma accumulate over a patient's life course, resulting from an interaction between the burden of stigmatization, physical and psychological comorbidities, coping strategies and external factors. The concept may help identify more vulnerable patients and facilitate more appropriate treatment decisions or earlier referrals. Although some potential risk factors for CLCI have been clarified, no all-encompassing screening tools are available. Patients at risk for CLCI should be identified by applying clinical, personal and psychosocial indicators and predictors individually. Early intervention in psoriasis treatment could improve long-term patient outcomes and modify the disease course. However, more research is needed to clearly define what constitutes 'early' intervention and to identify the most effective strategies for implementation. From a preventive point of view, it is helpful to identify early interventions aimed at reducing the risk of CLCI and establishing a new life course trajectory in patients with psoriasis. This review summarizes the latest developments in CLCI and psoriasis, highlighting knowledge gaps and future directions to make control of CLCI a possible goal for therapies.

Introduction

Cumulative life course impairment (CLCI) indicates the cumulative lifelong effects of stigmatization, physical and psychological comorbidities, and their economic and social consequences. These factors have the potential to place each patient with psoriasis at risk of not living their life to their full potential.[1,2]

The concept of CLCI was initially introduced for the assessment of psoriasis.[1] It was rapidly applied to other diseases that could potentially lead to life course impairment, including other dermatological conditions.[3–6] Given the relevance of CLCI in chronic diseases, the World Health Organization, in the Minsk Declaration, recognized that 'The adoption of the life-course approach across the whole of government would improve health and well-being, promote social justice, and contribute to sustainable development and inclusive growth and wealth in all our countries'.[7] Regrettably, the gravity of CLCI's impact on chronic diseases is not easily captured in clinical trials, which are typically of limited duration in comparison with a patient's lifespan.

This review provides an up-to-date definition of CLCI along with outcomes for improving the monitoring of patients with psoriasis, and highlights knowledge gaps. It focuses on identifying potential early interventions that might prevent its occurrence.

Cumulative life course impairment and psoriasis

Psoriasis is a chronic inflammatory skin disease with a strong genetic predisposition and autoimmune pathogenic traits.[8] In patients with psoriasis, inflammation typically involves the

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skin, the body's largest and most visibly prominent organ.[8,9] However, psoriatic inflammation may also affect the joints and different organ systems. Thus, it has been postulated that psoriasis is a systemic disorder rather than solely a dermatological disease.[8,9]

Compared with healthy individuals, patients with psoriasis may present increased hyperlipidaemia, hypertension, coronary artery disease, type 2 diabetes and body mass index.[9] The burden of these concomitant conditions, combined with the substantial stigmatization and reduced self-confidence due to cutaneous manifestations, can result in life choices that might have a lasting negative impact on a patient's life course.[9]

The cumulative impact varies from patient to patient based on the interplay of factors such as the burden of stigmatization, concurrent physical and psychological conditions, coping mechanisms over time, and modulation of external factors by the individual's personality.[10] Therefore, long-term consequences of psoriasis are not limited to physical impairment but may also include psychosocial factors. These include deterioration of personal and social relationships,[10] economic restrictions (e.g. psoriasis-associated expenses, difficulties in gaining and retaining paid employment, reduced working capability and productivity)[10,11] and, ultimately, psychological distress and behaviours that further worsen the disease.[10,12]

Identification of potential patients at risk of cumulative life course impairment

In 2013, a set of 11 risk factors that positively or negatively affect the life course of patients with psoriasis was introduced based on theoretical and clinical knowledge:[13]

- Clinical disease severity
- Chronic course of disease (disease duration)
- Early onset of psoriasis
- Perception of stigmatization
- Lack of social support
- Negative impact on profession
- 'Negative' mood/personality trait
- Coping strategy
- Quality of life
- Behaviours putting the patient at risk
- Comorbidities.

Clinical disease severity is usually evaluated by the Psoriasis Area Severity Index (PASI), body surface area or Physician's Global Assessment (PGA). It is directly related to CLCI, as low disease severity is associated with a lower risk of CLCI. However, there is considerable interindividual variation in how patients perceive their disease, even in the presence of objectively defined disease states. Moreover, the impact of clinical severity may be different when the disease appears in earlier periods of life.[13] Disease duration is another potential risk factor, as it may determine a longer time of exposure to potentially life-course-damaging elements. On the other hand, the chronicity of psoriasis could also lead to positive adaptation when coping behaviour is adequate.[13]

Early onset of psoriasis may affect patients in a more vulnerable phase, mainly if it occurs in children or young adolescents, when fewer intrapersonal coping mechanisms are available that might protect from CLCI.[14] A survey involving patients with psoriasis of different ages confirmed the CLCI burden in all age groups. An increased risk for incident suicidal ideation and limitations in the ability to do regular activities, such as studying and exercising, were reported by most young patients interviewed (median age 21 years).[14]

Almost 80–90% of patients reported some degree of psoriasis-related discrimination and stigmatization, which had negative effects on their professional careers and personal lives. Among these, up to 20% of patients with psoriasis have been banned from hairdressing salons, swimming pools or gyms. Reiterated episodes of discrimination may cause poor self-confidence, low social connection, and failure to achieve full life potential, a professional career or solid intimate relationships. Furthermore, feelings of low self-esteem and personal and social withdrawal caused by stigmatization might predispose them to develop psychological disorders and face a higher risk of addictive behaviours, including alcohol abuse, smoking, drug abuse and food dependency.[14] Social support may alleviate these risk factors, and diseases of any severity and duration can be better tolerated and coped with when family, friends or other people in a caring network support the patient.[13]

Psoriasis can also have a detrimental effect on education and professional life, as individuals with psoriasis tend to experience a higher number of missed days at work or school compared with healthy controls.[13] It has been reported that patients with psoriasis encounter difficulties finding or keeping a job, given lower productivity and loss of working time (days or hours) due to the management of flares, thus influencing a patient's potential to earn an income and gain full-time employment.[14] Positive emotions, such as optimism, trust, positive beliefs or joy, along with positive coping strategies, may compensate for risk factors for CLCI.[13] However, patients with psoriasis often experience anger, depression, grief, helplessness and loss of autonomy. Validated questionnaires such as STAI (State–Trait–Anxiety Index) or HADS (Hospital Anxiety and Depression Scale) can be used to assess patients' emotional status.[13]

The development of active coping strategies not only contributes to a more positive perception of the disease but also helps in avoiding other dangerous behaviours, including cigarette smoking, drinking and hyperalimentation. In addition to disease- and patient-related risk factors, there is also an increased risk of developing specific comorbidities due to the psoriatic, chronic inflammatory status. For instance, patients with psoriasis face an increased risk of metabolic syndrome.[13]

Valid measures of quality of life (QoL) should be routinely used to define treatment goals in practice. To evaluate the impact of psoriasis on QoL, the population-based Understanding Psoriatic Disease Leveraging Insights for Treatment (UPLIFT) survey was conducted, involving patients with mild-to-moderate psoriasis and their dermatologists.[15] Patients with at least one 'sensitive' area affected (scalp, face, genitalia, palms/nails, soles) reported a lower QoL, in particular when the face was affected. Approximately half of patients (52%) with psoriasis and/or psoriatic arthritis ($n=3806$) screened positive for potential major depressive disorder, according to the Patient Health Questionnaire (PHQ)-2 guidelines (i.e. PHQ-2 score ≥ 3).[15]

Genital psoriasis also has a relevant impact on QoL, as the disease can seriously impair patients' dating lives and relationships.[16] Up to 63% of adults with psoriasis experience psoriatic lesions on their genital area during their lifetime.[16] These issues determine embarrassment, stigmatization or shyness about this sensitive location, so patients might not discuss it even with their physicians during healthcare visits.[16] Furthermore, one-quarter of patients with psoriasis experience an impact on their sexual lives after the onset of psoriasis, regardless of gender. Sexual dysfunction is one of the causal factors in reducing QoL in patients with psoriasis.[17]

In summary, the impact of psoriasis on CLCI is multifactorial, and each factor has a particular relevance for the patient. Therefore, characterizing and listening to the patient is necessary to identify potential risk factors for CLCI and to address them promptly.

How to quantify cumulative life course impairment

The main difficulty in weighing each risk factor to quantify CLCI is their variability over time. To address this issue, important phases with long-lasting implications have been identified, such as education, forming partnerships and career development. Theoretical models have been described to differentiate between the 'critical period' and 'accumulation of risks' in the life course epidemiology of a chronic disease such as psoriasis. The first describes the long-term impact of risk factors acting in earlier critical periods, and the second refers to ongoing stressors resulting in cumulative damage.[2] Such models can also be applied to CLCI, taking into account that in children, adolescents and adults, the disease has a different impact, and this must be reflected in the quantification of CLCI.[2]

As described in the previous section, most of the identified risk factors are mainly clinical. It is noteworthy that CLCI may also be determined by psychological risk factors, such as perceived stigmatization, lack of coping strategies or resilience. However, there seems to be a considerable lack of data regarding psychological risk factors. Other aspects, such as lack of social support and impact on the ability to work, are not addressed at all. Further evidence is needed to obtain a comprehensive picture of the impact of all factors on CLCI.

Previous studies have utilized the Major Life Changing Decision Profile (MLCDP) and Life Changes Index Scale to assess impairments throughout the life of patients.[2] The MLCDP is a 32-item questionnaire with five domains: education, job/career, family/relationships, social and physical. It is not designed to measure change following intervention. For example, MLCDP could be used once every 5 years to determine whether the disease has affected any additional significant life-changing decisions. While MLCDP refers to how health conditions influence major life decisions, the Life Changes Index Scale assesses past or upcoming events. Neither measure captures how that impairment can cumulatively build, and both measures are generic rather than dermatology specific.[2]

The cumulative impairment of psoriasis is recognized through the additional questions in the novel tool DermCLCI-r (retrospective), referring to the ongoing burden and the life-changing impact of the condition.[18] This questionnaire consists of 30 items on retrospectively assessed impairments due to skin disease over the disease life course (e.g. burdensome symptoms of the disease, how to come to terms with the disease, coping strategies and average burden of disease at different ages). In parallel, DermCLCI-p (prospective) identifies the current CLCI status of the patient and future risks of developing irreversible damage (e.g. burdensome symptoms in the last 2 weeks). Both of these novel tools are under validation and could be of pivotal interest if they can distinguish between existing CLCI that cannot be undone anymore and the risk for future CLCI that should be prevented.[18]

In order to prevent CLCI progression, early detection of CLCI risk factors is crucial. As there are different risk factors increasing the CLCI of the individual patient, the screening tool should encompass elements of the psychological, clinical and personal spheres[13] through a multidisciplinary approach.

Multidisciplinary management of psoriasis to prevent progression of cumulative life course impairment

To prevent CLCI progression, a multidisciplinary life course approach can be applied to psoriasis management. By definition, the life course approach provides a framework that contributes to a better understanding of disease impairment in terms of both pathogenesis (when the disease and its course are seen as an outcome) and outcomes (when psoriasis is viewed as an exposure and impaired life course as the outcome).[19] According to the life course approach, life potential is impaired by the cumulative effect of risk factor exposures, which occur at different points in a person's life. These exposures will be modifiable, and risks can be reduced (i) via psychosocial interventions, such as patient education to improve coping behaviour and QoL, and support networks to facilitate social contacts; (ii) by the patient, for instance, by using effective coping strategies and by seeking social support; and (iii) by biomedical interventions.[19]

Comorbidities often related to psoriasis should be considered in a life course approach to reduce exposure to clinical CLCI risk factors. An observational study compared 17 683 patients with psoriasis with 10 000 patients without psoriasis included in the Danish National Patient Registry (1999–2013) and identified the diagnoses significantly associated with psoriasis within 5 years before or after the diagnosis.[20] The aim was to create a comorbidity trajectory network that could support clinicians conducting disease-risk analyses of patients with psoriasis and help plan optimal treatment to prevent future high-risk comorbidities. Four main comorbidity groups had a strong correlation with a psoriasis diagnosis: mental and behavioural disorders; diseases of the skin and subcutaneous tissues; diseases of the musculoskeletal system and connective tissue; and endocrine, nutritional and metabolic diseases.[20]

While the long-term impact of disease management requires further validation, effective early intervention could potentially alter the course of psoriatic disease and reduce its consequences on CLCI. Indeed, greater skin clearance was associated with a lower prevalence of alexithymia after

1 year of follow-up, reducing anxiety, depression and alcohol abuse.[21] Among the available approaches, biologic therapies were associated with reduced psychological distress and depression in patients with psoriasis,[22] reduced cardiovascular disease risk,[23] reduced risk for all-cause and cardiovascular mortality,[24] and reduced incidence of inflammatory bowel disease.[25]

The negative impact of psoriasis on patients can be modified via a shared decision-making process, consisting of both therapeutic management of the disease and related comorbidities, when present, and interventions with educational resources and tools aimed at promoting positive coping strategies.[1,10,19]

Multidisciplinary patient management should be advisable to prevent or reduce risk factors determining CLCI.[26] Therefore, dermatologists, psychologists and rheumatologists may collaborate to guarantee the most effective management of inflammatory symptoms in the skin and joints, and maintain their patients' QoL.[26] Working in coordination with the person experiencing psoriasis and their family or caregivers is fundamental to defining realistic goals and reaching optimal outcomes.[26]

Opportunity for early intervention

Early intervention with targeted therapies could beneficially affect the clinical course of psoriatic disease for many reasons. It may influence gene expression and the immune cells infiltrating the skin, thus directly acting on the inflammation underlying psoriasis; it may prevent psoriasis-related comorbidities, especially psoriatic arthritis; and it can improve patients' QoL and reduce CLCI (Figure 1).[14]

Randomized controlled trials have demonstrated that patients with psoriasis treated with targeted therapies had significantly improved QoL, measured with the Dermatology Life Quality Index (DLQI), compared with usual care.[14]

It seems plausible that in patients with moderate-to-severe psoriasis, prompt disease control may prevent the cumulative impact of psoriasis, physical, psychological and social, on a patient's life course.[14] However, some potential issues should be considered before implementing early intervention in routine clinical practice.[27]

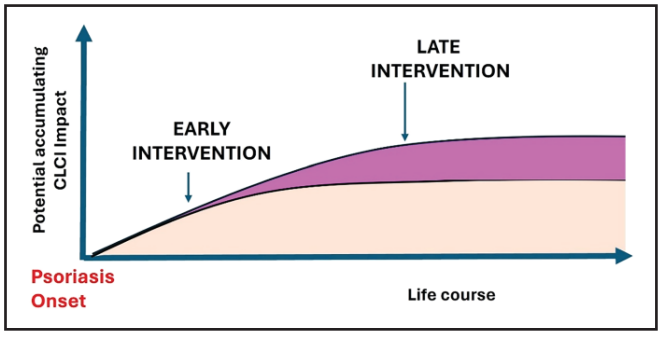

Figure 1 Early intervention may decrease the potential accumulating cumulative life course impairment (CLCI) during the life course. Earlier intervention will result in a lower impact of accumulating CLCI. The identification of potential candidates for early intervention, evaluation of CLCI risk factors, and monitoring of potential psychological and physical factors may contribute to limiting the impact of CLCI. The patient should be managed by a multidisciplinary team, which will determine disease control (≥ 90% improvement in Psoriasis Area and Severity Index, or Physician's Global Assessment ≤ 1), wellbeing (Dermatology Life Quality Index ≤ 1) and treatment burden (at most mild effects).[27–29]

Determining the concept of early intervention poses a challenge, as there is no universally accepted time interval from diagnosis for this aim. Generally, early-stage disease denotes the first 2 years from symptom onset for dermatological diseases. In contrast, a cutoff of 5 years has been used to distinguish between early and late treatment with biologics. In the case of psoriatic arthritis, the intervention is recommended as soon as the diagnosis is made. In the presence of plaque psoriasis, the unpredictable course of the disease and the development of complications make it challenging to base a definition of early intervention solely on time since diagnosis.[27] The age of onset of psoriasis might also be relevant in proposing a rationale for early intervention, given its association with clinical and psychological complications.[27]

A second issue is the identification of potential candidates for such intervention. In most cases, psoriasis is typically mild and can be managed with topical treatment alone; however, there can be considerable functional impairment from psoriasis even without irreversible or progressive skin damage. Risk factors should be attentively examined and looked for during visits to prevent comorbidities and CLCI.[27]

A third important consideration is establishing a clear definition of success for early intervention. This definition is essential for assessing the effectiveness and value of early treatment. Early intervention is not limited to controlling skin disease; it also aims to prevent complications, and long-term outcomes would be needed to validate its effectiveness. However, such outcomes are not collected in randomized clinical trials, and most of the information derives from retrospective observational studies.[27] Therefore, an early intervention to modify the course of psoriasis may be of outstanding importance, although further evidence and discussions are required.

Spanish updated recommendations for psoriasis management recognize that the impact of the disease on the whole course of a patient's life can be captured by the concept of CLCI. They suggest that clinicians should evaluate not only the current but also the potential future impact of the disease on each patient, by considering both sociodemographic factors (e.g. age and sex) and clinical variables, such as disease severity and comorbid conditions. CLCI should be regarded in clinical assessments and decisions about disease management.[28]

To monitor potential clinical signs or symptoms and risk factors of CLCI, a Belgian Delphi consensus experience applied the concept of a treat-to-target algorithm to psoriasis. This approach requires 'tight control' in the treatment of diseases, aiming to achieve predefined therapeutic targets within a limited timeframe. It includes strict follow-up from the patient and regular assessments of disease progression based on standardized measurements to determine disease control (PASI 90 or PGA ≤ 1), wellbeing (DLQI ≤ 1) and burden of treatment (at most mild side-effects). This approach also evaluates a domain beyond the skin by raising awareness of comorbidities and recommending that dermatologists actively refer to specialists if necessary.[29] Notably, the target for treatment should be adopted in each country according to local regulations and reimbursement criteria.[29]

An Italian Delphi consensus recognized the importance of long-term management of psoriasis and, contextually, the role of the retention rate of each systemic treatment.[30] Based on their experience and a literature review, the panel recognized a limited retention rate with conventional systemic therapies, primarily due to poor tolerability and metabolic adverse events. Biologic agents have a higher retention rate as their safety profile is more favourable, with the main reason for discontinuation being secondary inefficacy.[30] However, in Italy, biologic drugs can only be used second line after conventional therapies, including acitretin, ciclosporin, fumarates and methotrexate.[31]

Biologic drugs have dramatically changed the psoriasis treatment paradigm, enabling the establishment of new therapeutic goals with a focus on achieving PASI 90–100 (90–100% improvement from baseline). Consequently, they have led to a notable improvement of health-related QoL.[32] Indeed, it has been demonstrated that there is an inverse correlation between absolute PASI and QoL, in which low levels of absolute PASI are linked to improved health-related QoL, and even minimal residual disease could negatively affect patients' lives.[33] Among biologic drugs, the entire class of interleukin-23 inhibitors effectively treats the disease and enhances QoL.

Conclusions

Psoriasis impacts CLCI through various mechanisms. These include stigmatization, depression and other psychological factors potentially affecting the social and relational spheres, as well as physical factors, including itching, pain and arthritis, which may compromise daily activities. Given the systemic nature of psoriasis and its impact on social relationships, comprehensive and multidisciplinary patient management is advisable to achieve both clinical goals and CLCI modification.

A therapeutic alliance between healthcare providers, patients and caregivers might provide a personalized approach to treating the disease. Such an approach, based on listening during visits, appropriate disease control and psychological support, if accepted and required by the patient, is crucial to identifying risk factors for CLCI. This approach can identify potential candidates for early intervention aimed at modifying the course of the disease, especially given the lack of specific tools that can quantify CLCI.

Early intervention is recommended for patients exhibiting risk factors for CLCI and experiencing poor QoL, to control the disease and to improve long-term outcomes and health-related QoL. Among therapeutic interventions, biologic drugs can effectively improve QoL and reduce CLCI. However, further evidence is needed to better define the opportunity for an early intervention with biologic drugs to manage CLCI in patients with psoriasis.

Learning points

- Long-term consequences of psoriasis are not limited to a physical impairment. Psoriasis may also deteriorate personal and social relationships, determine economic outcomes and, ultimately, cause psychological distress and behaviours that further worsen the disease.
- Cumulative life course impairment (CLCI) indicates the cumulative lifelong effects of stigmatization and physical and psychological comorbidities.
- The negative impact of CLCI on patients with psoriasis can be modified via a shared decision-making process, consisting of both therapeutic management of the disease and interventions with educational resources and tools aimed at promoting positive coping strategies.
- Multidisciplinary patient management should be advised to prevent or reduce risk factors determining CLCI.
- Early intervention is recommended for patients exhibiting risk factors for CLCI and experiencing a poor quality of life.

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Conflicts of interest

L.M.H.A. has been a consultant and/or speaker for AbbVie, Almirall, Pfizer, Novartis and Janssen. D.D. has received fees from AbbVie, Janssen and Eli Lilly. S.D. has been a consultant or speaker for AbbVie, Almirall, Amgen, LEO Pharma and Novartis. G.M. has received fees from AbbVie, LEO Pharma, Sanofi and Eli Lilly. G.P. has received fees from AbbVie, Janssen and Pierre Fabre Pharma. S.P. has been a consultant and/or speaker for AbbVie, Almirall, Amgen, Eli Lilly, Janssen, LEO Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Sandoz and UCB. C.S.F. and M.M. have no conflicts of interest to declare. A.L., S.D.F. and B.Z. are full-time employees of AbbVie and may hold AbbVie stock and/or stock options.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Ethics statement

Not applicable.

Patient consent

Not applicable.

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CPD questions

Learning objective

To become more familiar with cumulative life course impairment (CLCI) in people with psoriasis.

Question 1

Which spheres in a patient's life does CLCI affect?

(a) Clinical outcome.
(b) Economic condition.
(c) Psychological condition.
(d) Social relationships.
(e) All previous answers are correct.

Question 2

Which risk factors negatively affect the life course of patients with psoriasis?

(a) Low Psoriasis Area and Severity Index (PASI).
(b) Only stigmatization.
(c) Presence of comorbidities and stigmatization.

(d) Presence of coping strategies.
(e) Presence of social support.

Question 3

How is CLCI quantified?

(a) By a blood examination.
(b) By personalized therapy, based on a therapeutic alliance between healthcare providers and the patient.
(c) By strong support between the patient and their social environment.
(d) By previously validated scales that unequivocally quantify CLCI.
(e) By radiological examination.

Question 4

Which therapeutic targets are monitored in the treat-to-target (T2T) algorithm for psoriasis?

(a) Disease control (PASI 90 or Physician's Global Assessment ≤ 1), wellbeing (DLQI ≤ 1) and burden of treatment (no more than mild side-effects).
(b) Only burden of treatment (no more than mild side-effects).
(c) Only lack of disease control.
(d) Psychological distress.
(e) Workability.

Question 5

What are the potential advantages of early intervention?

(a) Determining a short relief of disease symptoms.
(b) Limiting the therapeutic interventions to a short period of time.
(c) Only controlling skin disease.
(d) Only modifying the course of psoriasis.
(e) Preventing complications and modifying the course of psoriasis.

Instructions for answering questions

This learning activity is freely available online at https://oupce.rievent.com/a/PMKLQH

Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures.
- Reflect on the article.
- Register or login online at https://oupce.rievent.com/a/PMKLQH and answer the CPD questions.
- Complete the required evaluation component of the activity.

Once the test is passed, you will receive a certificate and the learning activity can be added to your RCP CPD diary as a self-certified entry.

This activity will be available for CPD credit for 5 years following its publication date. At that time, it will be reviewed and potentially updated and extended for an additional period.